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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769.420	01/26/2001	Sui Xiong Cai	1735.0440001/RWE/BEC	4240

26111 7590 01/24/2003

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EXAMINER

MCKENZIE, THOMAS C

ART UNIT PAPER NUMBER

1624

DATE MAILED: 01/24/2003

12 ✓

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/769,420

Applicant(s)

CAI ET AL.

Examiner

Thomas McKenzie Ph.D.

Art Unit

1624

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 07 January 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: \_\_\_\_\_.
- Claim(s) objected to: 39,41,59 and 61.
- Claim(s) rejected: 33-38,40,42,43,46,47,51,52,58,60,71 and 76.
- Claim(s) withdrawn from consideration: \_\_\_\_\_.
8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☒ Other: PTO-892 attached

This action is in response to amendments filed on 1/7/03. Applicants amended claims 33, 42, 43, 46, 47, 58, and 76. Applicants cancelled claims 45, 49, 50, 53-57, 72-75, and 77. In the previous office action objection was made to claims 59 and 61. All other pending claims were rejected. There are twenty-one claims pending and twenty-one under consideration. Claims 58-61 are compound claims. Claim 71 is a composition claim. Claims 33-43, 46, 47, and 76 are use claims. This is the third action on the merits. The application concerns some nicotinamide compounds, compositions, and uses thereof.

***Response to Amendment***

Applicants' listing of the diseases they intend to treat overcomes the indefiniteness rejections made in point #5 of the Final-Rejection. Applicants' listing of their intended prodrug compounds overcomes the indefiniteness rejection made in point #6. Applicants' amendments, changing claim 76 to a method claim and the reference to what is substituted, overcomes the indefiniteness rejection made in point #7. Applicants' listing of the diseases they intend to treat also overcomes the enablement rejection made in point #8. Applicants' amendment listing the specific cancers they intend to treat overcomes the enablement rejection made in point b#9. Applicants' deletion of claims 53 and 56 renders moot the enablement rejections made in points #10 and #11. Applicants' cancellation of

claim 74 and amendment to claim 76 renders moot the written description rejection made in point #14.

***Claim Rejections - 35 USC § 112***

Claims 33-38, 40, 42, 43, 46, 47, 51, 52, 58, 60, 71, and 76 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The provisos in the last ten lines of claims 33, 42, 46, the last three lines of claim 34, and the last two lines of claim 58 lack description. Nowhere in the specification is such a relationship linking the description among radicals R<sup>1</sup> through R<sup>11</sup> described. Such a negative limitation requires description. In *Ex parte Grasselli, et al.* 231 USPQ 393, decided June 30,

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1983, the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences said: "we agree with the examiner's position of record that the negative limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112." "It might be added that the express exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts."

***Claim Rejections - 35 USC § 102***

Claim 58 remains rejected under 35 U.S.C. 102(b) as being anticipated by Setliff (Proc. Arkansas Acad. Sci.) for reasons cited in the previous action. A complete copy of this reference is included with the present action. The compound previously discussed is compound **IVi** in Table 1, page 93.

Claims 58 and 71 remain rejected under 35 U.S.C. 102(b) as being anticipated by Yagihara ('385) for reasons cited in the previous action.

Claims 33, 34, 36, 38, 42, and 46 remain rejected under 35 U.S.C. 102(b) as being anticipated by Gammill ('075). Compound **16** of the reference anticipates Applicants' use claims and fits formula (III) with  $R_6 = R_7 = R_9 = R_{10} = \text{hydrogen}$ ,  $R_1 = R_4 = R_5 = \text{hydrogen}$ , and  $R_2 = R_3 = 4\text{-morpholinyl-4H-benzopyran-4-on-6-yl}$ . The compound is found in lines 54-55, column 20. Activity against cancer, arthritis, and psoriasis is disclosed in in lines 11-24, column 16.

Claims 33, 36, and 38 remain rejected under 35 U.S.C. 102(a) as being anticipated by Kubota (WO 99/19303 A1). There is one compound in this reference, which anticipates Applicants' use claims. It is entry 36 on page 36. It and fits formula (III) with  $R_6 = R_7 = R_9 = R_{10} = \text{hydrogen}$ ,  $R_1 = R_2 = R_4 = R_5 = \text{hydrogen}$ , and  $R_3 = 3,5\text{-bis(trifluoromethyl)-1H-pyrazol-1-yl}$ . An English traslation of this reference is included with the present action. Activity against

inflammations and articular rheumatism (rheumatoid arthritis) is taught in the first sentence on page 8 of the translation. See also claims 13 and 14 of the translation.

Claims 33 and 38 remain rejected under 35 U.S.C. 102(b) as being anticipated by Clemence ('140). There is one compound in this reference, which anticipates Applicants' use claims. The compound was cited previously and fits formula (III) with  $R_6$  = hydroxy,  $R_7$  = trifluoromethyl,  $R_9 = R_{10}$  = phenyl and  $R_1 = R_2 = R_3 = R_4 = R_5$  = hydrogen. It is Example 4, lines 13, column 10 to line 43, column 11. Activity against rheumatoid arthritis is taught in claim 15 of the reference.


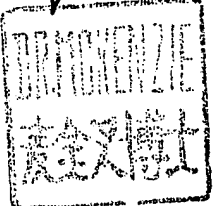
Claims 33, 36, 38, 42, and 46 remain rejected under 35 U.S.C. 102(e) as being anticipated by Mantlo ('884). There are over one hundred compounds disclosed in this reference, which anticipate Applicants' use claims. One compound was previously cited and fits formula (III) with  $R_6 = R_7 = R_{10}$  = hydrogen,  $R_9$  = phenylamino,  $R_1 = R_2 = R_4 = R_5$  = hydrogen, and  $R_3$  = methoxy. The compounds are found in Tables 8-13, spanning columns 84-91. See also compound claims 1-15 in this reference. Activity against rheumatoid arthritis is taught in line 36, column 96 of the reference. Activity against inflammatory bowel disease and psoriasis is taught in line 40-41, column 96. Activity against cancer is taught in line 57, column 96.


Applicants' new provisos referred to above, exclude anticipatory compounds. However, the provisos are new matter and the anticipation rejections are maintained.

***Allowable Subject Matter***

Claims 39, 41, 59 and 61 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

TCMcK  
January 22, 2003

  
JOHN M. FORD  
PRIMARY EXAMINER  
GROUP - ART UNIT 1624